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SCIENCE

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May 10, 1848.

Sir:

The Association of American Geologists and Naturalists, at its Meeting in Boston, on the 24th of September, 1847, resolved itself into the American Association for the Promotion of Science, elected its Officers as such, and appointed the time and place of the first Meeting under the new organization and more extended plan of operations, to be in the City of Philadelphia, on the third Wednesday (20th) of September, 1848, at 10 o'clock A.M.

As it is desirable to secure the attendance, on this occasion, of all who feel an interest in the progress of Science, and in advancing the purposes of the Association, the Local Committee have directed us to invite your attendance, and to request that you will, if convenient, prepare a paper on such branch of Science as may best accord with your own views. If unable to be present at the Meeting, it is still hoped that you will favor the Association with a communication, to be read in your name by the Secretary.

Whether you can attend or not, you are respectfully requested to return an answer, post paid, to this invitation, addressed to the Chairman of the Association, Philadelphia, together with the title of any communication you may desire to make, by the 1st of September, or as early as may be convenient, that suitable arrangements may be made for the Meeting.

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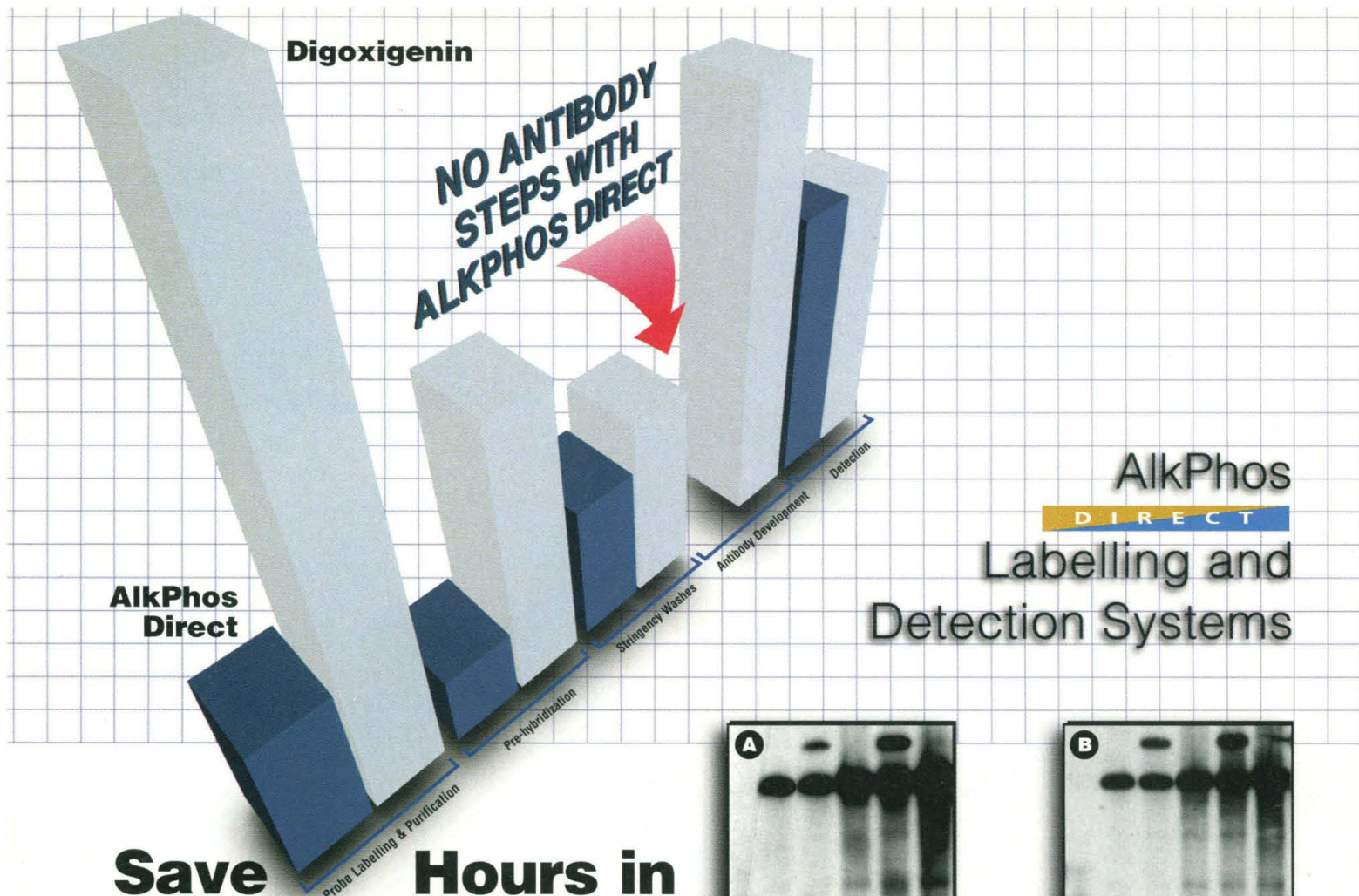
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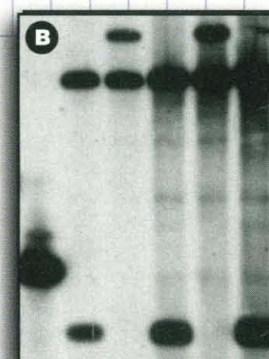
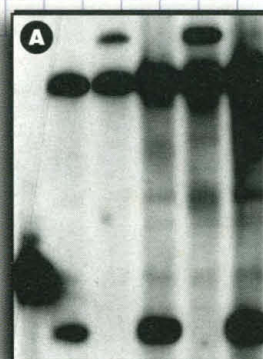
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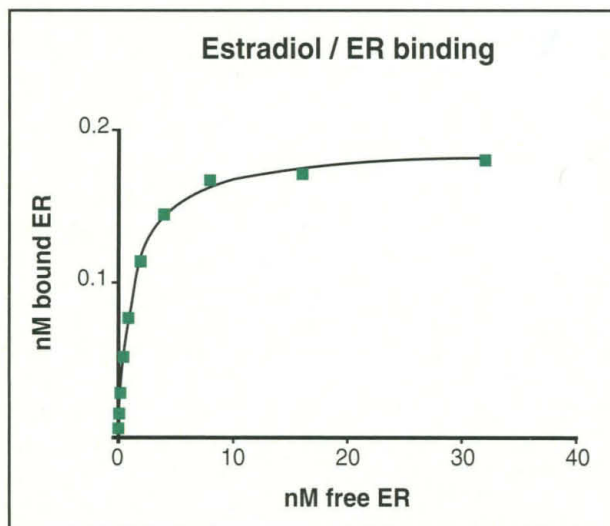
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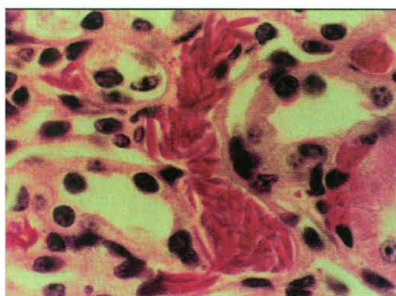


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Son of Adam



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Mouse model for sickle cell disease

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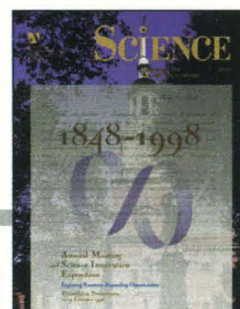
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COVER

The invitation to the first meeting of what was then planned to be the American Association for the Promotion of Science. Independence Hall is pictured in the background. AAAS will open its 150th Anniversary year celebration with the Annual Meeting in Philadelphia,

where the association was founded on 20 September 1848 at the Academy of Natural Sciences. See page 885 for the many special activities and speakers that will be a part of the 1998 opening. [Photo of Independence Hall: Photodisc, Incorporated. Collage: C. Faber Smith]



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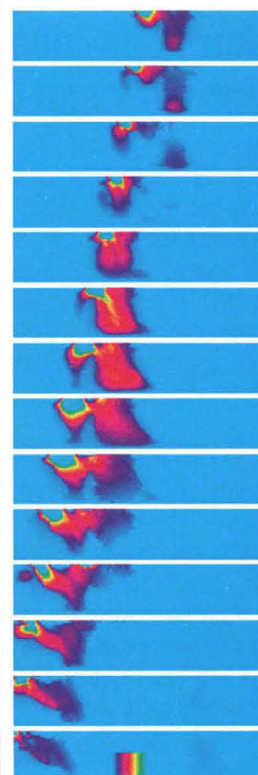
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834

Yikes! Here comes the rupture

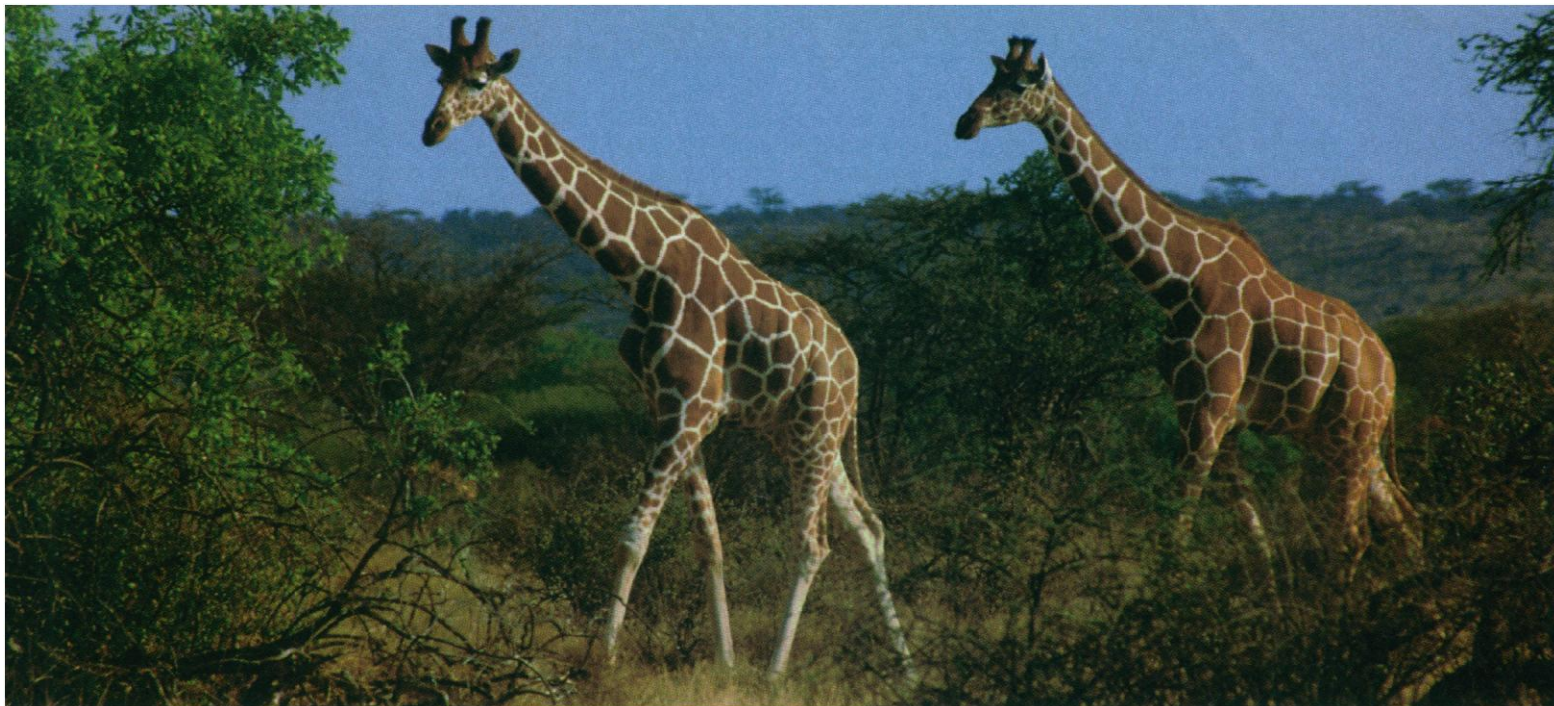
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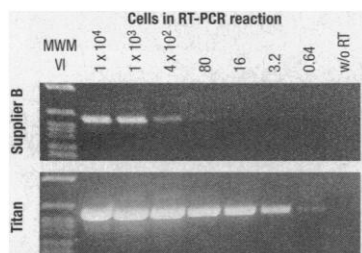


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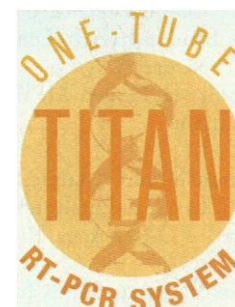
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THIS WEEK IN SCIENCE

edited by PHIL SZUROMI

Mesoporous metal films

Mesoporous materials that contain nanometer-sized pores have received considerable attention recently. Most of these materials that have been made are ceramic oxides. Attard *et al.* (p. 838) now report the synthesis of mesoporous platinum films by electrodeposition of the metal from liquid-crystalline plating mixtures. Such materials could be used in applications that include catalysis, batteries, fuel cells, and sensors.

Suddenly warmer

The end of the Younger Dryas marked the abrupt (about 40-year) transition to warm climates in the Holocene; this transition has been studied closely as it provides information on the sensitivity of Earth's climate. Taylor *et al.* (p. 825) analyzed the GISP2 Greenland ice core, which provides a year-by-year account of the climate changes, and shows that this transition occurred in a series of steps each lasting less than 5 years. Some data imply that climate changes in the Arctic slightly follow changes at lower latitudes.

Re-creating an earthquake

The 1992 Landers earthquake in the Mojave Desert is one of the best-characterized recent events; surface deformation could be readily measured in the desert, and seismicity was monitored before and after this magnitude 7.3 earthquake. Olsen *et al.* (p. 834) used the slip and stress distribution derived from inverting the seismic data to re-create the initial stress distribution in the area before the earthquake and then forward-modeled the rupture in three dimensions. Their rupture model fits the general pattern of ground motions from seismic recordings but also shows

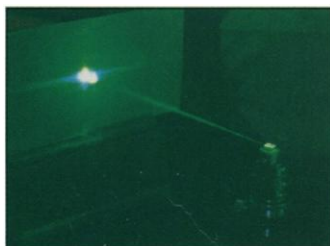
Mouse models for sickle cell anemia

Animal models for human diseases have been valuable for understanding the disease and designing effective therapies. Two separate groups, Pászty *et al.* (p. 876) and Ryan *et al.* (p. 873) have developed a strategy that resulted in a mouse model for sickle cell anemia (see the news story by Barinaga, p. 803). They first created mice that carried human sickle hemoglobin and then bred them with mice in which the mouse forms of α and β globin had been deleted. Progeny were identified that expressed only human hemoglobin and showed sickling of red blood cells, anemia, and organ pathologies that are characteristic of the human disease.

a complex process that includes an increasing rupture velocity as the rupture approaches the surface, which was not predicted by simpler kinematic inversions.

Quasi-periodicity in nonlinear optics

Structures that repeat not on the basis of rational numbers, such as crystals, but that repeat on the basis of irrational ratios, are quasi-periodic. Zhu *et al.* (p. 843) show that the formation of layers of a nonlinear optical material, lithium tantalate, with a quasi-periodic (Fibonacci) sequence



is useful in generating third-harmonics of laser light. The availability of more wave vectors in such a lattice allows coupling of two processes, frequency doubling and frequency adding, so that the normally weak third harmonics can be generated efficiently.

Copper chaperone in the cell

Certain enzymes in mammalian cells require metals such as copper as cofactors. However, free

copper can be toxic to the cell and propagate auto-oxidation of lipids, proteins, or nucleic acids. Pufahl *et al.* (p. 853; see the Perspective by Valentine and Gralla, p. 817) describe the function of a copper chaperone protein called Atx1, which receives copper from an uptake protein in the membrane and then binds it in an unusual three-coordinate state as Cu(I). The Atx1 protein then carries the copper to its destination where Atx1 interacts with the vesicular protein Ccc2. The Cu(I) ion is passed to Ccc2 and ultimately to the multi-copper oxidase Fet3, the essential enzyme in the high-affinity iron uptake system. This system allows the cell to supply copper to key enzymes without the release of copper ions directly into the cytoplasm.

Aerosols and smog production

Photochemical smog, characterized by high ground-level ozone and nitrogen oxide levels, depends partly on the intensity of solar ultraviolet radiation. Atmospheric aerosols scatter or absorb ultraviolet light, but a quantitative analysis of this effect on smog formation has been lacking. Numerical modeling by Dickerson *et al.* (p. 827) of observations of aerosols, radiation, and photochemistry indicate that smog production is accelerated by ultraviolet-scattering aerosols and inhibited by ultraviolet-absorbing aerosols.

Responding indirectly

Previous assessments of global terrestrial responses to climate change have focused on direct responses to change in carbon dioxide or temperature. These near-instantaneous responses include, for example, the effects of increased temperature on photosynthesis and respiration. However, field ecologists have repeatedly suggested that indirect responses, such as feedbacks through soil water storage or nutrient cycling, may be more important. Braswell *et al.* (p. 870; see the news story by Williams, p. 802) offer a global assessment of direct versus indirect effects, and demonstrate the importance of indirect effects. The results also provide evidence at the global scale for major differences between biomes in both the direction and strength of these indirect effects: Large-scale modification of global ecosystems could alter the response of the biosphere to climate change.

Cytokines and NF- κ B

The transcription factor NF- κ B is critical for regulation of gene transcription in cells of the immune system. Two reports discuss identification of a new component of a regulatory pathway that controls the activity of NF- κ B in response to cytokines like tumor necrosis factor- α or interleukin-1 (see the Perspective by Maniatis, p. 818). NF- κ B is held in an inactive state by the protein I κ B, and interaction of the two proteins is controlled by phosphorylation of I κ B. A protein kinase (I κ B kinase or IKK-1) that participates in this regulation has been recently described. Mercurio *et al.* (p. 860) and Woronicz *et al.* (p. 866) now report isolation and characterization of a second member of the IKK family (IKK-2). The two IKKs interact with each other and with another protein kinase, NIK, in a large protein complex.

WHAT IF YOU COULD CREATE A DRUG THAT WAS INACTIVE UNTIL IT WAS “SWITCHED ON” AT THE TARGET SITE?

Doctors want drugs powerful enough to destroy a disease. But they also seek to leave healthy parts of the body unharmed.

Much of medicine is an unending search for a delicate balance between these contrary goals.

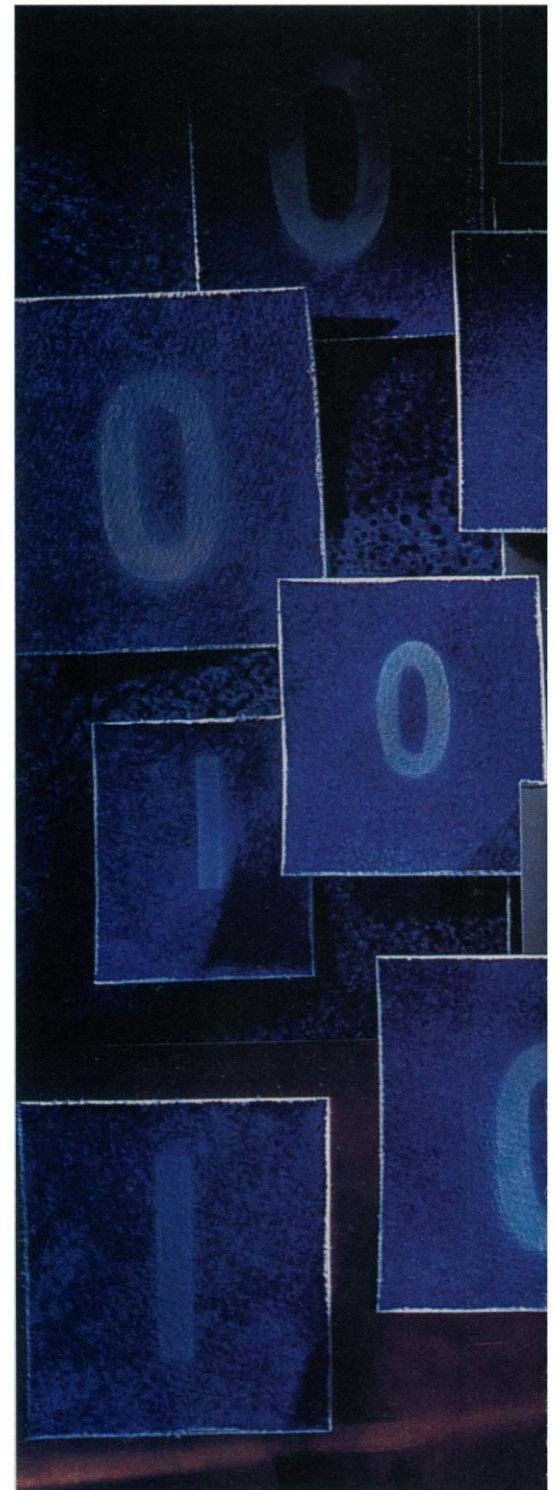
But what if we just turned the problem on its head?

What if we had a drug that could flow freely throughout the body without affecting normal tissue, and then “turn on” only when and where it was needed? And what if it only required a low-power, non-thermal red light for activation?

This is the vision of PhotoPoint,[™] a dramatic new medical procedure being developed by Miravant. It may give medical practitioners a high degree of selectivity and control in a minimally invasive procedure.

PhotoPoint may have application for a wide range of conditions ranging from cancers to eye diseases, and is now being tested in preclinical and clinical studies in the U.S. and internationally.

We’ll be telling you more about PhotoPoint in the months to come. Stay tuned.



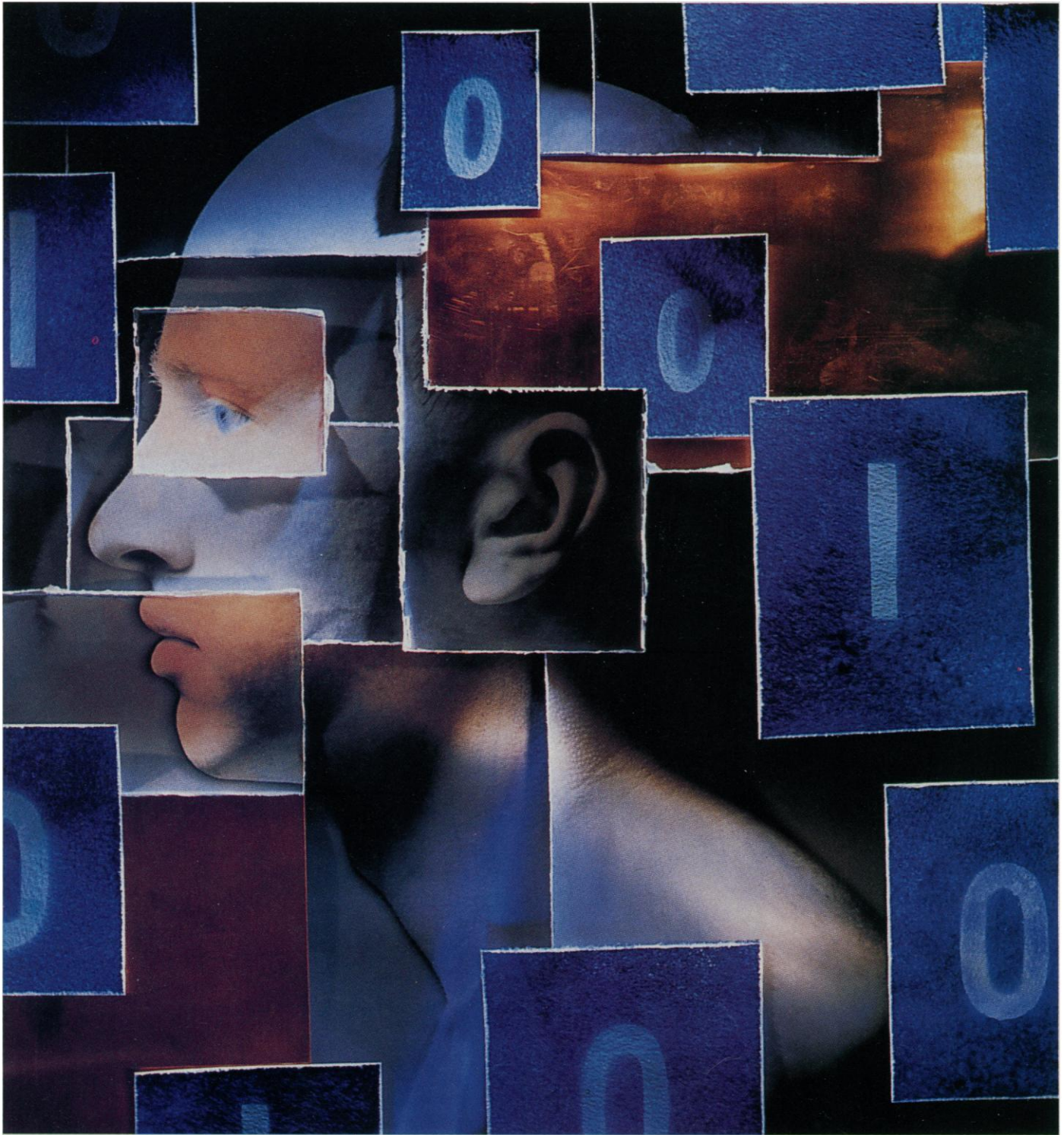
PhotoPoint has potential to selectively target a range of abnormal tissues in the body, such as diseases like cancer or retinal abnormalities.



In clinical studies, the PhotoPoint drug is injected and is subsequently retained by target cells. It remains inactive until exposed to a specific wavelength of non-thermal red light.



Light is directed at the target area. A small diode-based system generates the light, and special devices deliver it within the body or on its surface.

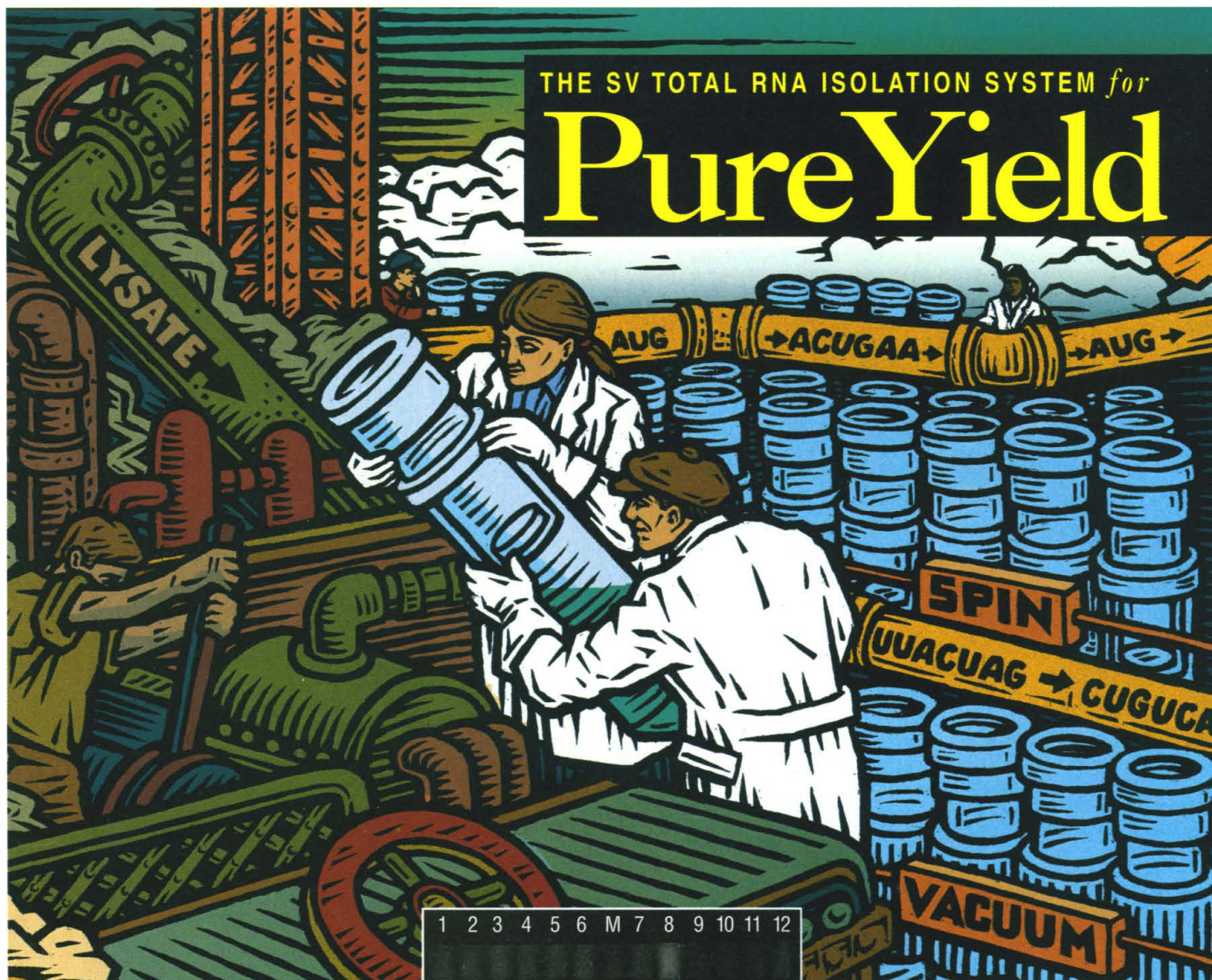


Targeted cells are destroyed by an interaction between the drug and the light, with minimal known side effects. PhotoPoint, now in clinical trials, is being developed as an outpatient procedure.

Learn more about PhotoPoint™ and Miravant (Nasdaq: MRVT) at www.miravant.com, or call toll-free at 888-685-6788. The company's products require U.S. Food and Drug Administration approval before marketing.



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Now isolate high quality
total RNA with
Promega's unique
"SV" (Spin or
Vacuum) technology!



Formaldehyde Gel Electrophoresis of RNA.
RNA was isolated from 30mg liver tissue using Promega's system (Lanes 1-6) and a competitor's system (Lanes 7-12). Promega's system yielded an average of 100µg consistently. The competitor's system yielded an average of 70µg with wide variability. (M = marker lane)

SV Total RNA Isolation System

- High yields of pure RNA
- Choice of spin or vacuum
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- No chromosomal DNA contamination
- Fast protocol with no phenol

Product Information

Product	Cat.#
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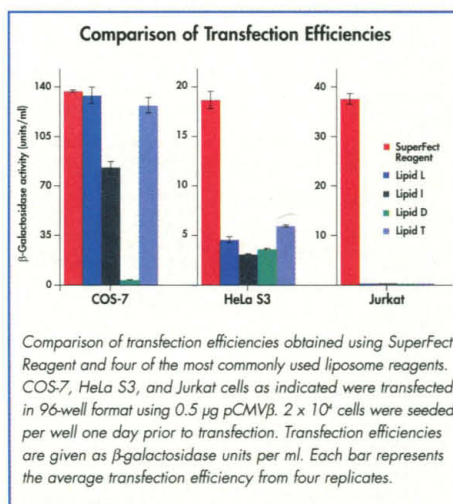
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Proven DNA Polymerase with Greater Processivity and Higher Fidelity.
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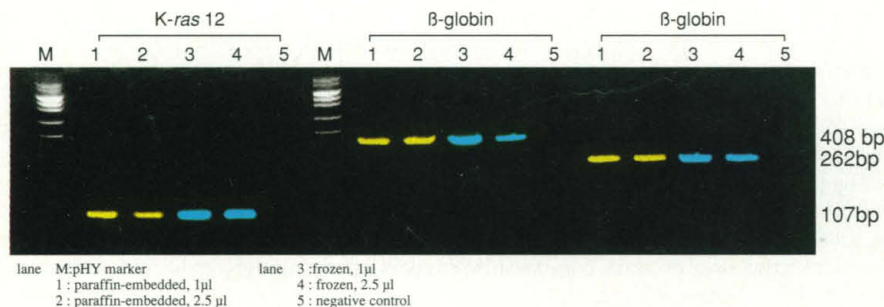
*U.S. Patent 5,436,149 for LA Technology Owned by TAKARA SHUZO CO., LTD

DNA Amplification from Histologic Sections

With DEXPAT™, DNAs were extracted as PCR ready templates which were then amplified with ExTaq to result in excellent PCR amplification with greater yield and longer extension than the conventional method.

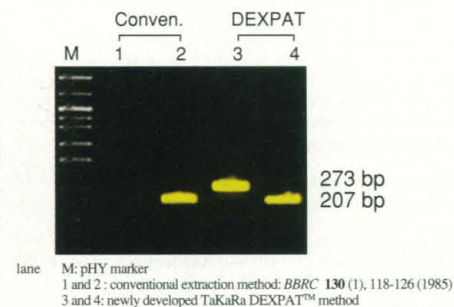
Comparison of Section Preparations

for K-ras 12 (107 bp) and β-globin (408 bp and 262 bp) Amplification from Human Tonsil: 1 μl or 2.5 μl extracts used for 25 μl PCR



Comparison of Extraction Methods

for p53 exon 5 (273 bp) and exon 6 (207 bp) Amplification from Paraffin-embedded Tissues of Colon Cancer After a 10-year Preservation



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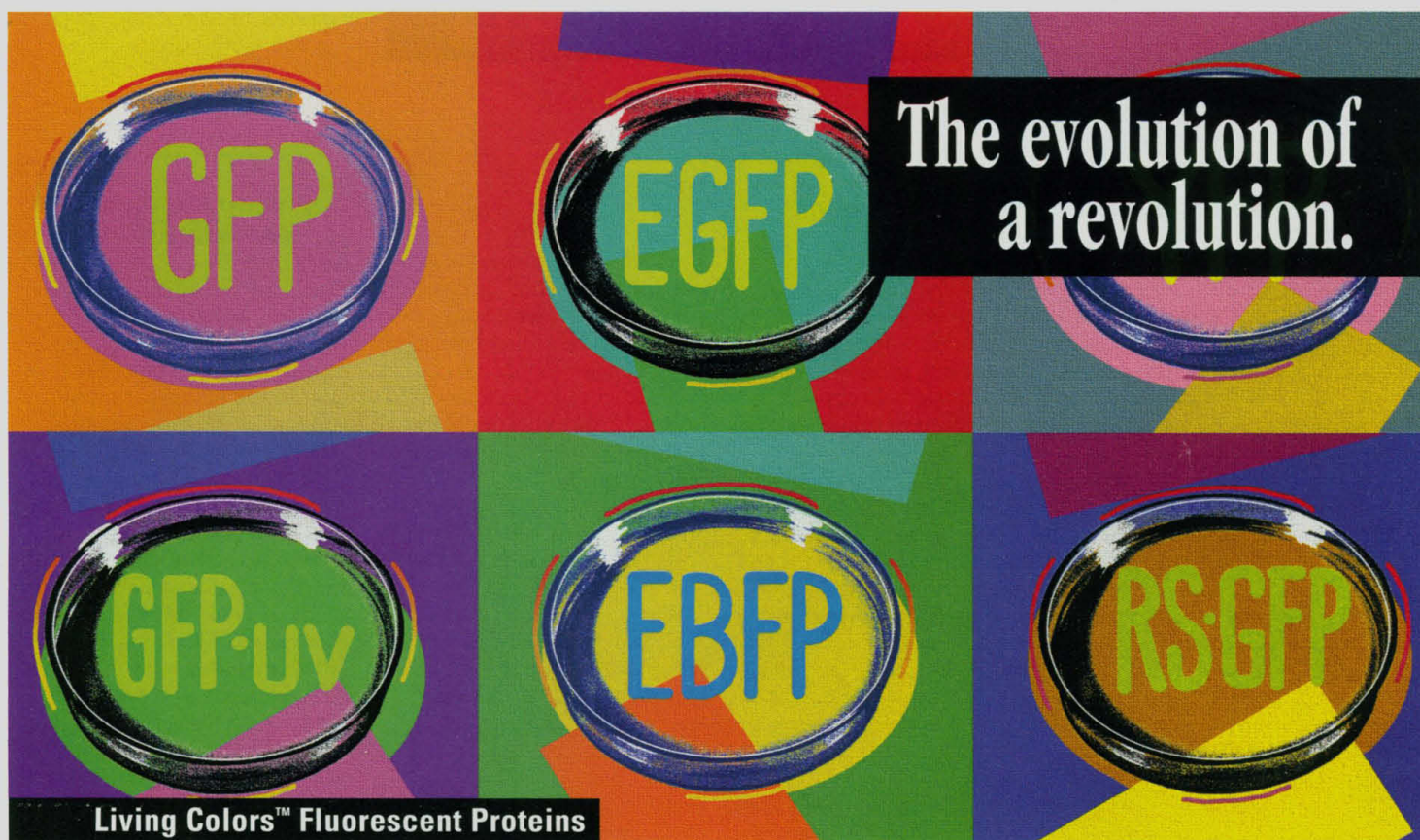
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CENTER FOR INHERITED DISEASE RESEARCH

The Center for Inherited Disease Research (CIDR) is a resource to provide high throughput genotyping services to research efforts that are attempting to identify genetic loci and allelic variants involved in human disease. CIDR concentrates primarily on multifactorial hereditary disease in humans although linkage analysis of single gene disorders can also be accommodated. Using samples provided by the principal investigators, CIDR carries out genome-wide scans for parametric and non-parametric linkage analysis using automated fluorescent technology to detect microsatellite markers with ~10 cM average spacing. Consultation on study design and statistical analysis are available as additional, and optional, services to investigators. The data and analyses will remain the property of the principal investigator and, once the studies in CIDR are complete, will be returned to the principal investigators for further research.

CIDR is a joint effort by eight participating institutes at NIH: the National Cancer Institute (NCI), the National Human Genome Research Institute (NHGRI), the National Institute of Child Health and Human Development (NICHD), the National Institute on Deafness and Other Communication Disorders (NIDCD), the National Institute on Drug Abuse (NIDA), the National Institute of Environmental Health Sciences (NIEHS), the National Institute of Mental Health (NIMH), and the National Institute of Neurological Disorders and Stroke (NINDS). CIDR is located at the Bayview Research Campus of the Johns Hopkins University and is operated by the university through a contract from the NIH.

For a special introductory period, investigators whose projects are supported by one of the eight NIH Institutes participating in CIDR will receive free genotyping. Other investigators supported by an NIH institute not participating in CIDR or from another governmental or non-profit institution will be charged \$1.00 per genotype (DNA sample x microsatellite marker).

Access to CIDR is open to all investigators on a competitive basis through peer review. For a more complete description of CIDR, including specific application procedures, visit our Website at <http://www.cidr.jhmi.edu/>. If you would like additional information, contact Dr. Jerry Roberts, Scientific Review Administrator and Executive Director, CIDR Board of Governors, in the NHGRI Office of Scientific Review.

Application Deadlines

* November 1 ■ March 1 ■ July 1

Jerry Roberts, Ph.D.
National Institutes of Health
National Human Genome
Research Institute
38 Library Drive MSC 6050
Building 38A, Room 609
Bethesda, MD 20892-6050
(301) 402-0838
FAX (301) 480-2770
jerry_roberts@nhgri.nih.gov



* The November 1997 deadline has been extended to November 15

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UPCOMING TOPICS

Tech.Sight publishes every third Friday of each month and offers readers a chance to see the future of science. Upcoming topics include:

17 OCT: Structure-activity relationships by nuclear magnetic resonance—its impact and use, along with combinatorial chemistry and pharmacokinetics, on rational drug design
Space reservation deadline: 26 September

21 NOV: Single Cell Laser Microdissection
Space reservation deadline: 29 October

19 DEC: Animal Models for AIDS Research
Space reservation deadline: 26 November

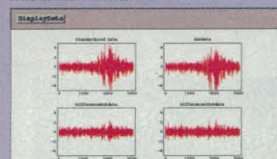
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From the *Mathematica*® Applications Library—

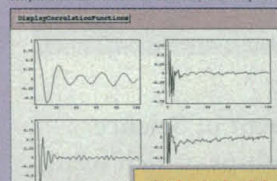
A Fully Integrated Environment for Time-Dependent Data Analysis

Exploration of Seismic Data from the Kobe Earthquake

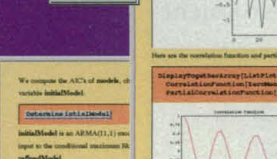
To render the data stationary we have logarithmically detrended it, standardized it to zero mean and unit variance (N.R. = "Standardized Logarithmically Detrended"), and then computed the difference series yielding the original data plus the three associated time series, N.R. Data, DifferenceN.R. Data, and Difference2N.R. Data.



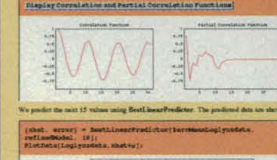
The primary portion of the data shows a pronounced peak at around 140 and a low point near 500, corresponding respectively to approximate periods of 22 and 5.5 seconds. These periodicities can also be seen in the correlation functions, which are now plotted.



We compute the AIC's of models, fit various initial models. InitialModel is an ARMA(1,1) model input to the conditional maximum likelihood method. The result is a smaller model, refittedModel. The Hannan-Rissanen method is used to fit a model, refittedModel. The correlation and partial correlation functions of refittedModel are quite similar to the original data.



The correlation and partial correlation functions of refittedModel are quite similar to the original data. We predict the next 15 values using BestLinearPredictor. The predicted data are shown in the plot below.



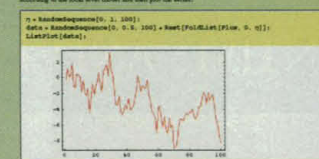
Plotting the correlation and partial correlation functions of the predicted data, we see that they are quite similar to the original data.



YuleWalkerEstimate
LevinsonDurbinEstimate
BurgEstimate
InnovationEstimate
HannanRissanenEstimate
ConditionalMLEstimate
MLEstimate
LongAREstimate
LogLikelihood

Kalman Filtering and Kalman Smoothing

To illustrate the use of the Kalman filter, we generate a series according to the first level model with $R = E^2 = 0.5$ and $Q = E^2 = 1$. With these parameters we generate a time series of length 100 according to the first level model and then plot the series.

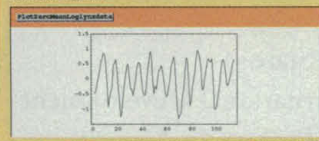


E_1 and P_1 , used as the starting values for KalmanFilter, are computed as follows:

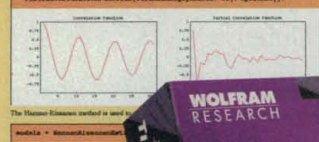


An Analysis of the Lynx Data Set

We model the population data recorded for the number of lynx trapped annually in northwest Canada from 1821 to 1934. We first take the Log of the data, detrend, and remove its mean. The result is called ZeroMeanLogLynxData.



Here we use the correlation function and partial correlation function for the Lynx data set out to a lag of 30.



The Hannan-Rissanen method is used to fit a model, refittedModel. The correlation and partial correlation functions of refittedModel are quite similar to the original data.



We predict the next 15 values using BestLinearPredictor. The predicted data are shown in the plot below.



Models

- Stationary time series models: AR, MA, ARMA
- Nonstationary time series models: ARIMA, SARIMA
- Univariate and multivariate time series models
- Structural models: State-space form and the Kalman filter
- ARCH and GARCH models
- Covariance, correlation, and partial correlation functions

Model Identification

- Estimation of sample covariance, correlation, and partial correlation functions
- Akaike's Information Criterion (AIC)
- Bayesian Information Criterion (BIC)

Parameter Estimation

- Yule-Walker, Levinson-Durbin, Burg's, innovations, and long autoregression algorithms
- Hannan-Rissanen procedure
- Maximum likelihood method

Diagnostic Checking

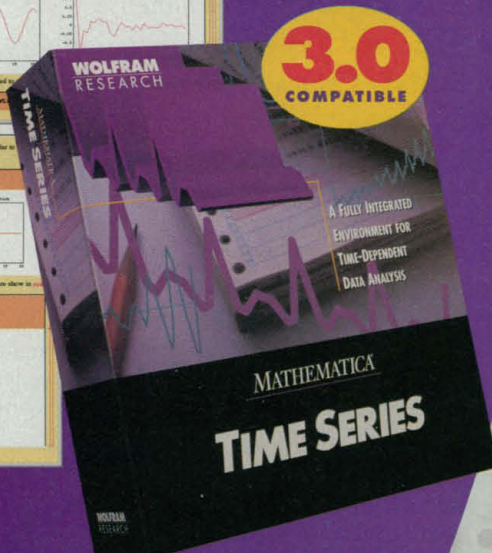
- Residuals
- Portmanteau test
- Information matrix

Forecasting

- Exact and approximate best linear predictor
- Updating the prediction

Spectral Analysis

- Spectra of ARMA models
- Spectrum estimation
- Smoothing spectrum using lag and spectral windows



To find out more about *Time Series* and other products in the *Mathematica* Applications Library, visit
<http://www.wolfram.com/applications/tsx>
 or call toll free 1-888-576-8673

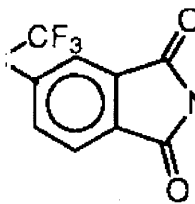
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For further information and application instructions, contact:

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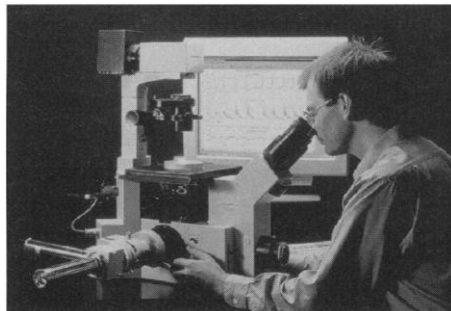




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The PhoCal/PhoClamp photometric system offers true 32-bit functionality under Windows 95. The system provides fast photon counting and photometric acquisition to give quantitative fluorescence and luminescence measurements of intracellular fluorescent probes. It is available as a fully integrated system or networked for off-line use. Collected data can be exported to popular spreadsheets, databases, or graphics programs. The system enables up to four-

PRODUCTS



wavelength photometric measurements of intracellular optical probes. It provides real-time measurement of fast or slow changes in fluorescence, luminescence, or other light output arising from chemical probes for ions, antigen markers, receptor probes, and other reagents. It can be used with all currently available optical probes. **Olympus.** For information call 800-446-5967 or circle 141 on the Reader Service Card.

Genomic DNA Purification

The MasterPure Kit can purify genomic DNA that is ready for polymerase chain reaction (PCR) from human or other mammalian blood in less than 30 min without resins, columns, or hazardous reagents. The purified DNA can be used directly in PCR amplification or Southern blotting. Applications include rapid screening for mutations or genetic markers, detection of alleles, and determining pedigrees. **Epicentre Technologies.** For information call 800-284-8474 or circle 142 on the Reader Service Card.

Photon Counting Systems

Two new photon counting systems combine the latest advances in avalanche photodiode technology with the counting capability of the Model T914P multichannel scaler to facilitate the recording of weak optical signals as a function of time. The systems, which differ only in their dark current specifications, consist of an avalanche photodiode detector module, a multichannel scaler, a computer interface card, operating software,

and interconnecting cables. This combination eliminates many of the disadvantages found in systems using photomultiplier tubes, for example, the danger from cables carrying high voltages and susceptibility to electromagnetic interference. The detector modules are self-contained and incorporate thermoelectric cooling to provide the user with single photon detection capability at very low dark count rates. **EG&G Signal Recovery.** For information call +44 (0) 118 977 3003 or circle 143 on the Reader Service Card.

Gene Analysis Software

DNASIS for Windows 2.5 is a new version of a gene analysis software program. It includes a direct interface to the Internet NCBI BLAST database. Searches can be initiated within DNASIS and results opened in either a text file or as an HTML file. Advanced primer design functions have been added. A file converter permits data to be shared between labs with different DNA sequence analysis packages. **Hitachi Software Engineering America.** For information call 415-615-9600 or circle 144 on the Reader Service Card.

Image Analysis Software

Version 2.0 of 1D Image Analysis Software is available for Macintosh and Windows systems. The software acquires digital images from Kodak Digital Science cameras or any TWAIN compliant scanner and can be used for analyzing DNA, RNA, and protein electrophoresis gels and blots. Analysis data includes mass, molecular weight, intensity, and mobility values. New features include automated lane finding, non-destructive annotations, Gaussian band fitting, and enhanced printing capabilities. **Eastman Kodak.** For information call 800-225-5352 or circle 145 on the Reader Service Card.

HPLC Syringe Filters

GD/X syringe filters for high-performance liquid chromatography are for preparing small volumes of difficult samples that would clog most conventional filters. GD/X syringe filters offer a comprehensive range of membranes suitable for aqueous and organic samples. But in addition to the filtering membrane, each housing includes a prefiltration stack of graded density glass microfiber. This prefiltration stack removes larger particles from the sample, leaving the final membrane filter to remove the fine particulate materials

to the desired size, with less hand force than with traditional syringe filters. **Whatman International.** For information call (01622) 676670 or circle 146 on the Reader Service Card.

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Literature

REGEN Regenerated Cellulose Membrane is a product sheet on cassettes for processing hydrophobic proteins, for processes that have already been validated with regenerated cellulose, and for processes involving the use of harsh solvents. These membrane cassettes exhibit high flux rates for faster processing times. **Pall Filtron.** For information call 800-345-8766 or circle 148 on the Reader Service Card.

Wako Technical Update describes new products for 1997 and highlights products that have generated increased interest in recent months. The focus is on molecular biology products, inhibitors, antibodies, enzymes, assay kits, and unique standards. **Wako BioProducts.** For information call 800-992-9256 or circle 149 on the Reader Service Card.

Pure Water Handbook, a guide to water purification technologies, explores the overall problems of water purity, identifies common impurities, and discusses popular methods of purification. **Osmonics.** For information call 800-848-1750 or circle 150 on the Reader Service Card.

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